Citation:

Lopez S, Bermudez B, Pacheco YM, Villar J, Abia R, Muriana FJ. Distinctive postprandial modulation of beta cell function and insulin sensitivity by dietary fats: Monounsaturated compared with saturated fatty acids.*Am J Clin Nutr.* Sep 2008; 88 (3): 638-644.

PubMed ID: 18779278

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether postprandial glucose homeostasis is modulated distinctly by high-fat meals enriched in saturated fatty acids (SFAs) or monounsaturated fatty acids (MUFAs).

Inclusion Criteria:

- Male
- Adults
- BMI less than 25kg/m^2
- Normal blood count and serological measures
- Non-smokers, not consuming special diets, taking vitamins, antioxidants or medication
- No history of medication known to affect lipoprotein metabolism or insulin secretion or its activity.

Exclusion Criteria:

- Younger than 18
- BMI>25kg/m^2
- They displayed biochemical evidence of renal impairment, hypothyroidism or liver dysfunction.

Description of Study Protocol:

Recruitment

Subjects were recruited by advertising.

Design

Randomized controlled, single-blind, cross-over within subject design.

Dietary Intake/Dietary Assessment Methodology

- Subjects consumed test meals along with a portion of plain pasta (30g/m^2 body surface area), one slice of brown bread and one container of skim yogurt
- Subjects were placed in NCEP diet for two weeks before the beginning of the trial
- Each cycle included one week of the NCEP diet in between test meals as a washout and adaptation period
- The planned carbohydrate, protein, and fat distribution was similar for all high-fat diets
- To avoid aberrant lipid metabolism that could interfere with postprandial triglyceride handling, the glycemic index of the carbohydrate-containing foods and the glycemic load of the meals was low, approximately 20 (25% of the glycemic load of 75gOGTT)
- The average total energy provided by the meals was approximately 800kcal (approximately 10kcal per kg), and the macronutrient profile was as follows: 72% fat, 22% carbohydrate and 6% protein
- The subjects also consumed the same test meal containing no fat as a control meal
- Subjects kept personal dietary records (mentioned in reference 13), but these were only used for patient compliance.

National Cholesterol Education Program (NCEP) Step I diet (control diet)

- 50g/m^2 body surface area of butter, ratio MUFA:SFA (0.48:1.0)
- Refined olive oil (ROO), ratio MUFA:SFA (5.43:1.0)
- High-palmitic sunflower oil (HPSO), ratio MUFA:SFA (2.42 :1.0)
- Mixture of vegetable and fish oils (VEFO), ratio MUFA:SFA (7.08:1.0).

Statistical Analysis

- The summary data (the fasting and postprandial response) for glucose, insulin, triglycerides, and FFAs were analyzed by using one-factor repeated-measures analysis of variance
- The postprandial time courses after the test meals were analyzed by using two-factor repeated-measures analysis of variance with interaction, and a Bonferroni correction was applied for the post hoc detection of significant pairwise differences
- Areas under the curves were calculated for glucose, insulin, triglycerides and FFAs with the trapezoidal rule
- A Pearson correlation was used to explore the strength of the association between postprandial estimates of β-cell function and insulin sensitivity with the ratio of MUFAs to SFAs in dietary fats.

Data Collection Summary:

Timing of Measurements

- After ingestion of the meal, blood samples were collected in tubes containing EDTA each hour to measure glucose, insulin, triglyceride, and FFA concentrations over eight hours. Thus, nine blood samples were collected over a 480-minute period after the ingestion of a mixed meal
- In this study, each participant served as his own control.

Dependent Variables

- Plasma glucose and triglyceride concentrations were measured on a Hitachi Modular Analytics D-2400 analyzer using commercially available reagents and an enzyme-based kit
- Plasma insulin was measured using a specific enzyme-linked immunosorbent assay on a Hitachi Modular Analytics E-170 analyzer
- Plasma FFA concentrations were measured by using an ACS-ACOD assay on a COBAS Mira-Plus analyzer
- Empirical index: The insulinogenic index (IGI), as a surrogate measure of first-phase insulin

secretion, was calculated as the difference between the postprandial insulin peak (measured at 60 minutes) and basal insulin in relation to the difference in glucose
- Empirical Index: Ratio of the IGI to the HOMA-IR, which gives an adjusted measure of β-cell function that accounts for variations in insulin sensitivity
- Empirical index: Ratio of the insulin to glucose areas under the curve (AUCI/AUCG) is significantly correlated with glucose sensitivity and it is a parameter that describes the secretory process of β-cells
- Empirical Index: The HOMA-B was also used and β-cell function was assessed during the meal intervention by extending the values of HOMA-B to those at 60 minutes
- To measure basal insulin resistance and sensitivity authors used three surrogate measures of insulin-mediated glucose disposal:
    - HOMA-IR (I0 x G0/22.5)
    - The revised-quantitative insulin sensitivity check index (rQUICKI=1/[log I0 + log G0 + log FFA0]
    - The basal insulin sensitivity (IS) index (ISI0) for glycemia and blood FFAs proposed by Belfiore
    - To measure postprandial insulin sensitivity authors used three surrogate indexes of IS during the intervention:
        - An IS index (IS0-∞) according to an integral equation model
        - An oral glucose IS index (OGIS0-∞)
        - The postprandial IS index (ISI0-∞) for glycemia and blood FFAs
- Such indexes were denoted as ISGTTTM, OGISGTTTM, and ISIGTTTM, respectively.

Independent Variables

Dietary manipulation with five different diets containing specific amounts of monounsaturated, saturated and polyunsaturated fatty acids.

Control Variables

- Age
- BMI.

Description of Actual Data Sample:

- *Initial N:* 14 male
- *Attrition (final N):* 14 male
- *Age:* 27±7 years
- *Ethnicity:* Not described
- *Other relevant demographics:* None described
- *Anthropometrics:* BMI=23.9±1.9kg/m^2
- *Location:*
    - Cellular and Molecular Nutrition, Instituto de la Grasa (CSIC), Seville, Spain
    - University Hospital “Virgen del Rocío”, Seville, Spain.

Summary of Results:

- There were no differences in the mean plasma glucose, insulin, triglyceride and free fatty acids (FFA) concentrations between the subjects at fasting

- There were no significant (NS) differences in the basal values for homesotasis mean assessment for b-cell and insulin resistance (HOMA-B and HOMA-IR), the revised-quantitative insulin sensitivity check index (rQUICKI), and the basal Belfiore indexes for glycemia and blood FFAs. This means that subjects had a similar basal β-cell function and insulin sensitivity before intervention with different meals
- Control meal (non-fat) did not induce any postprandial lipemic response
- The postprandial glucose response was similar after ingestion of the five diets including the control
- The AUC for insulin and FFAs were positively and well correlated (P<0.001) with the AUC for triglycerides
- The empirical indexes of postprandial β-cell function were all significantly higher after the high-fat meals than after the control meal (P<0.01), including the IGI, IGI/HOMA-IR, and AUCI/AUCG during the zero to 120- and zero to 480-minute GTTTM and the HOMA-B at the 60-minute GTTTM. These indexes increased in conjunction with the increase in the proportion of SFAs in the dietary fats
- Estimates of postprandial insulin sensitivity were found significantly lower values (P<0.001) for ISGTTTM, OGISGTTTM, and the postprandial Belfiore indexes for glycemia and blood FFAs after the high-fat meals than after the control meal. These estimates decreased in conjunction with the amount ofSFAs in the dietary fats
- All of the indexes calculated for β-cell function and insulin sensitivity during the intervention showed a strong and significant correlation with the ratio of MUFAs to SFAs in the dietary fats (P<0.001).

Author Conclusion:

Data suggest that β-cell function and insulin sensitivity progressively improve in the postprandial state as the proportion of MUFAs with respect to SFAs in dietary fats increases.

Reviewer Comments:

- *This was a well conceived and executed randomized, cross-over, single-blinded controlled trial*
- *Extrapolation of the results should be considered with care as this was very small clinical study that included young healthy, non-overweight men only*
- *The reviewer found most of the missing information related to the characteristics of the experimental diets in the following citation (13 within this article):*
    - *Pacheco YM, Bermudez B, Lopez S, Abia R, Villar J, Muriana FJG. Ratio of oleic to palmitic acid is a dietary determinant of thrombogenic and fibrinolytic factors during the postprandial state in men. Am J Clin Nutr 2006; 84: 342-349.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes